National Aeronautics and Space Administration

THE LIFETIME SURVEILLANCE OF ASTRONAUT HEALTH Newsletter

Volume 26, Issue 1

Editor's Note: This volume of the newsletter will discuss several different ways that Lifetime Surveillance of Astronaut Health (LSAH) is assisting NASA with assessing the human systems risks, from the development of a new concern to integrating several related risks into one consolidated risk. This work contributes to decreasing the health and performance risks faced by our astronaut corps in space exploration.

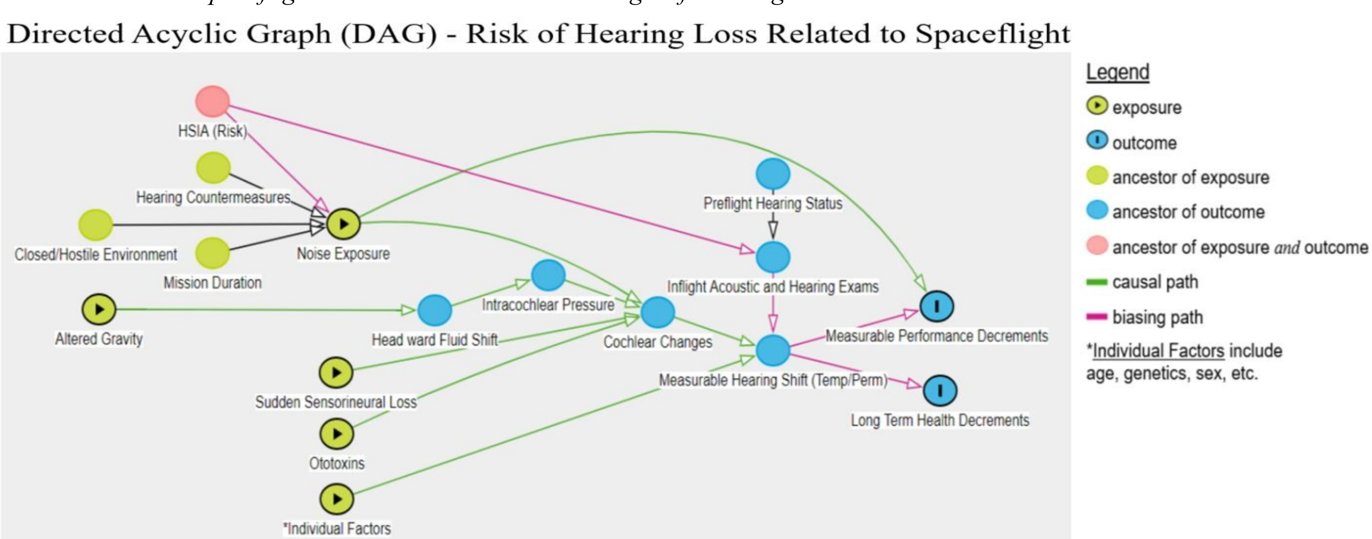
Human Systems Risk Board: An Introduction

Jacqueline Charvat, Ph.D.

The Human Systems Risk Board (HSRB), which is jointly chartered by the Human Health and Performance Directorate and the Office of the Chief Health and Medical Officer (OCHMO), manages all human system risks pertaining to crew health and performance for space missions, which includes pre, in, and post-flight risks and long term health. Through a continuous risk mitigation process, the HSRB facilitates the understanding and communication of human system risks that can affect astronauts' health and performance both in flight and after their time at NASA. HSRB decisions and recommendations are used to guide the medical, scientific, and technology development activities to mitigate the risks. Currently, the HSRB tracks 28 active risks and one concern pertaining to astronaut crew health and performance. A "risk" is a health or performance issue supported by evidence that requires mitigation; a "concern" is an issue being monitored to evaluate if it should become a full risk. The HSRB risks relate to many different aspects of living in space such as environmental exposures, performance issues, biomedical stressors, the ability to provide medical care, and other challenges that affect the astronaut's ability to successfully complete their mission.

There are two types of consequences of the human systems risks: operational risks during a mission

Figure 1.
A Directed Acyclic Graph (DAG) is a tool that the Human Systems Risk Board is using to show the relationships between spaceflight hazards and possible mission outcomes, as well as the interconnectedness of the different risks. The DAG displayed below shows how spaceflight hazards could lead to hearing shifts among the crewmembers.



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Human Systems Risk Board: An Introduction continued

and long-term health consequences from spaceflight exposures. The mission and operational drivers to human system risks include: environmental exposures such as the changes in gravity; the distance from earth where real-time communications and the ability to return to Earth are limited; and spacecraft constraints such as the ability to remove carbon dioxide from the vehicle atmosphere. The long-term health of the crewmember is also a key component to understanding human systems risks. Some risks, such as risk of electric shock or the risk of inadequate team dynamics, are mainly relevant during a mission and long-term post-mission effects are not expected. Conversely, some risks are driven by the expected long-term health consequences that could occur, such as risk of degenerative disease due to radiation exposure.

Risks are always present during spaceflight. They can and should be understood, managed, and mitigated to reduce threats posed to the astronauts. Risk management in the context of human spaceflight can be viewed as a trade-based system. The relevant evidence in life sciences, medicine, and engineering is tracked and evaluated in order to identify ways to minimize overall risk to our astronauts and to ensure mission success. The HSRB creates a management framework for human systems risks by applying a mission scenario and assigning an evidence-based likelihood and consequence score for different mission types and lengths (known as Design Reference Missions). This framework enables the principles of Continuous Risk Management and Risk-Informed Decision Making to be applied and allows NASA management to see which risks need additional research or technology development in order to be mitigated or monitored.

HSRB evaluates each of the risks on a two-year cycle. A risk package is generated based on information and data that support the risk posture, then the package is presented to the board. Data are re-evaluated periodically and new information is integrated into the risk package. Along with the Human Systems Risk Manager, a team of risk custodians comprised of a researcher, an operational researcher or physician, and a Lifetime Surveillance of Astronaut Health (LSAH) epidemiologist, develops each risk package. This group works together to understand and synthesize scientific and operational evidence in context of spaceflight, identifies and evaluates metrics for each risk in order to communicate the risk posture to the agency, and makes recommendations on reducing the risk. The LSAH epidemiologists are integral members of the risk custodian teams – in Fiscal Year 2020 the epidemiology team contributed over 2000 hours to 13 risk presentations. Epidemiologists have specific skills in population data gathering, analysis, and interpretation, such as creation of Directed Acyclic Graphs to visualize the relationships between risks and health outcomes (see Figure 1, Page 1) . This work contributes to decreasing the health and performance risks faced by our astronaut corps in space exploration.

The Concern for Venous Thromboembolism during Spaceflight

Jacqueline Charvat, Ph.D., Sara Mason, B.S.

NASA's understanding of human system risks evolves with spaceflight experience, research, and terrestrial medicine. For example, during a mission NASA identified a new health issue: a crewmember on the ISS had a venous thromboembolism (VTE) of the internal jugular vein discovered during a vascular ultrasound performed for a research study.[1] This adverse event was reported to the NASA Institutional Review Board. Upon review, it was found that among 11 research participants, the mean cross-sectional area and pressure of the internal jugular vein increased during spaceflight compared to preflight measurements. Stagnant or reverse blood flow in the internal jugular vein was also observed in over half of the study participants.[2] A Lifetime Surveillance of Astronaut Health (LSAH) review of astronaut medical data found no additional VTE diagnosed within 90 days of returning from flight.

Collectively, venous clots and emboli are called VTE. Deep vein thromboses (DVT) are blood clots occurring in a major vein in the human body (see Figure 2, Page 3) . On Earth, upper extremity DVT are rare compared to lower extremity DVT. Most upper extremity DVTs are related to catheteriza-

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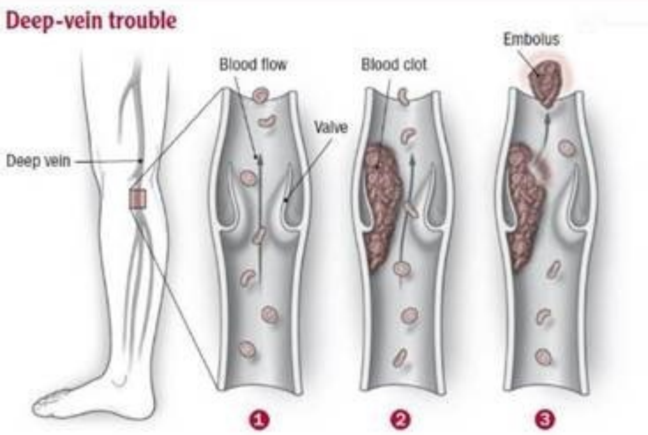
The Concern for Venous Thromboembolism during Spaceflight continued



❶ Leg veins contain small valves that help keep blood moving toward the heart. Injury, immobility, and other factors can lead to the formation of a blood clot ❷ inside a leg vein. This is called a deep-vein thrombosis. Sometimes a piece of the clot breaks away ❸ (this is called an embolus) and enters the circulation. If it lodges in the lungs, it can cause a potentially deadly pulmonary embolism.

Figure 2.
Deep vein thromboembolism
Source: https://www.health.harvard.edu/heart-disease-overview/deep-vein-thrombosis-overview

tion, anatomic abnormalities, or repeated physical exertion. Upper extremity DVT occur in veins such as the subclavian vein in the shoulder or jugular vein in the neck. DVT pose a health risk because clots can break apart from the original site, move through the bloodstream, and block blood flow in major organs. This is called an embolus or embolism. A common site for an embolus is the lungs, which is referred to as a pulmonary embolism. Annually, there are about 900,000 new diagnoses of VTE in the United States.[3]

On Earth, the risk of VTE typically increases as people get older. Other risk factors include hospitalizations, major surgery, trauma, fracture, or cancer as these conditions can lead to stagnant blood flow. DVT have been seen in astronauts during medical exams, but the data reviewed by LSAH showed that the DVT diagnosed among astronauts up to five years after spaceflight were likely provoked by injury, illness, or surgery. Other terrestrial risk factors for VTE, such as elevated body mass index or other medical comorbidities, tend not to apply to astronauts who have undergone rigorous selection and athletic training.

In women, a large risk factor for the formation of VTE is the use of combined oral contraceptives. Female astronauts may decide to suppress menstrual cycles during training and spaceflight with the use of this medication. Levels of certain markers in the blood such as hemoglobin, hematocrit, or iron stores may also contribute to the development of VTE.[4] Another study compared these terrestrial biomarkers as risk factors for VTE in female astronauts who used oral contraceptives during flight to those that did not use them.[5] At the time of the review, no VTE had been diagnosed during spaceflight. The authors also showed no trend in the biomarkers that would increase the risk of VTE in female astronauts taking oral contraceptives.[5] As further occupational surveillance and research data are collected, these biomarkers and risk factors can be monitored to understand if astronauts are at additional risk for VTE.

These research and clinical findings have shed light on a previously unknown risk in human spaceflight. Because it is so new, NASA is working to expand the research and occupational surveillance measures to gain a better understanding of the formation of clots during spaceflight. As this evidence is gathered, NASA is maintaining the possible development of VTE as a Human Systems Risk Board (HSRB) “concern.” NASA has implemented new clinical practice guidelines and surveillance protocols for monitoring clot formation via vascular ultrasounds to collect data before, during, and after a mission.

NASA does not yet know to what degree the unique environment of spaceflight increases the risk for VTE. As new data are derived from occupational surveillance and research, the HSRB concern will be updated. Data from occupational surveillance and research will allow the HSRB risk custodians to decide whether the issue should remain a concern, develop into a full risk, or close the concern if it is deemed not a risk to astronauts. These data will be pivotal for the prevention and treatment of VTE in microgravity, especially as longer missions to the Moon and Mars are planned.

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The Concern for Venous Thromboembolism during Spaceflight continued

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Systematic Review of Cancer Outcomes and the Evidence Base

Ruth A. Reitzel, Ph.D.

As a part of a broader agency-wide review of radiation exposure standards led by the Office of the Chief Health and Medical Officer (OCHMO), the Lifetime Surveillance Astronaut Health (LSAH) team began a systematic review of our existing evidence base and terrestrial literature to better understand the incidence and outcomes of cancers in the astronaut population. As of December 31, 2017, LSAH had recorded 238 cancer cases (171 cases non-melanoma skin cancer) in the astronaut population, contributing to 20 deaths. While risks of cancer in the astronaut population are similar to the U.S. general population, astronauts have unique occupational risk factors, including radiation exposure due to space flight.[1]

The U.S. Department of Veteran Affairs (DVA) has identified a number of diseases as potentially radiogenic (caused or worsened by radiation exposure), including various cancers, cataracts, non-malignant thyroid nodular disease, parathyroid adenoma, tumors of the brain and central nervous system, and amyotrophic lateral sclerosis.[2] Each of these conditions have different latency periods, preventative screenings, diagnoses, treatments, and prognoses. As a result, understanding the overall picture of these diseases in astronauts requires that each condition be evaluated independently.

In 2020, LSAH began to expand upon the internal LSAH evidence base for cancers and conditions associated with exposure to radiation through a systematic review of peer-reviewed medical and scientific publications. A systematic review of this literature is based on a pre-defined protocol and study aims. Standardized review methods are implemented for literature searching, article selection, article review, and data abstraction.[3] This differs from a typical literature review as it systematically considers the entire body of literature to answer a specific question.

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Systematic Review of Cancer Outcomes and the Evidence Base continued

For each of the conditions identified by DVA, LSAH systematically reviewed the medical literature with the following goals:

- To evaluate the published literature for changes in incidence, prevalence, or mortality over time of the cancer/condition in the U.S. general population;
- To evaluate the published literature for changes in incidence, prevalence, or mortality over time of the cancer/condition in the populations such as U.S. military and civilian air crew that may be more comparable to the NASA astronaut population;
- To assess the impact of changes to preventative screening recommendations on the prevalence and mortality of the cancer/condition.

A systematic review is more intensive than a traditional review of the scientific literature. A broad search strategy was used to identify the relevant literature for each condition, thus reducing the potential for missing relevant articles due to too narrow of a search strategy. Subsequently, LSAH epidemiologists screened thousands of titles and abstracts resulting from the broad search in order to narrow down the articles that could potentially answer the research questions (typically 50-100 publications). The full texts of these publications were then reviewed and subjected to a second round of pre-defined inclusion/exclusion criteria to further narrow down literature. Data was abstracted from articles that were included (typically 25-50 articles) (see Figure 3). This data was then synthesized and compiled to build the expanded evidence base.

Understanding of this evidence base will allow for a better characterization of the cancer incidence in the NASA astronaut population. The systematic reviews and incidence of cancer within the astronaut corps will contribute to the OCHMO review of radiation exposure standards. Results of systematic reviews and cancer incidence updates will be published in future issues of the LSAH newsletter.

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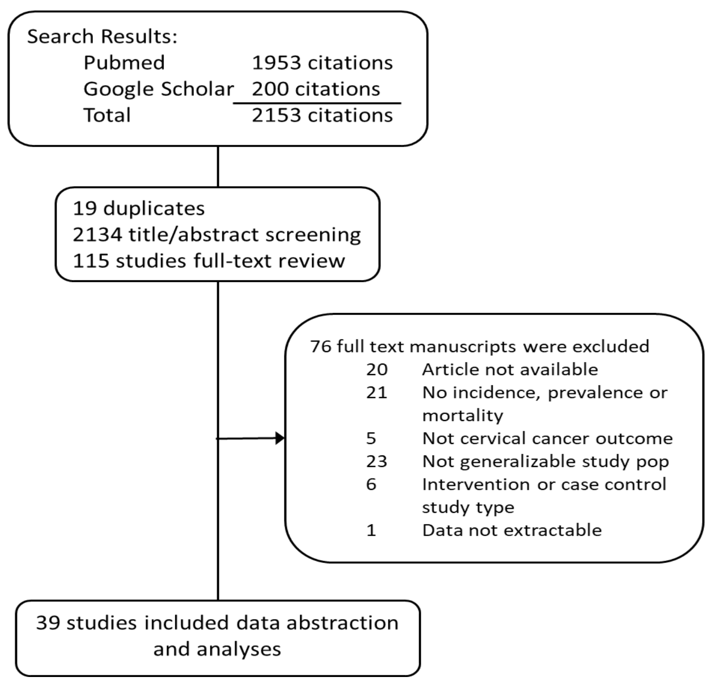

Figure 3.
This PRISMA flow chart demonstrates the systematic flow of how articles were included, full text reviewed, and potentiality excluded to reach the number of studies that were included in the final data abstraction and analyses.

COVID-19 and LSAH Exams

Mary Wear, Ph.D.

COVID-19 (officially known as Severe Acute Respiratory Syndrome Coronavirus 2 or SARS-CoV-2) has altered daily life across the globe. As of January 1, 2021, approximately 350,000 Americans have lost their lives to the novel virus. To protect the health of our former astronauts, NASA has paused in-person annual Lifetime Surveillance of Astronaut Health (LSAH) exams. Since we are unsure when it will be safe to return to normal operations, planning is underway for conducting modified LSAH exams using a combination telehealth visit and diagnostic tests performed at labs near your home rather than at the Johnson Space Center Flight Medicine Clinic. Our current goal is to have planning completed and a program implemented in early 2021. Former astronauts who participate in the LSAH study will be notified when these remote LSAH exams become available.

In addition, behavioral health telehealth visits with the Flight Medicine Clinic (FMC) Clinical Neuropsychologist, Dr. Carmen Pulido are now available. This is the first time behavioral telehealth services have been offered at the FMC. To schedule a telehealth visit with Dr. Pulido, please contact Amy Trabue at Amy.L.Trabue@nasa.gov.

There are many reliable sources of information about COVID-19:

- CDC main page for information around COVID-19:
  Centers for Disease Control (CDC): Coronavirus Disease 2019 (COVID-19)
- A dashboard with global and national data about the pandemic and critical trends:
  Johns Hopkins Coronavirus Resource Center
- Global information about COVID-19:
  World Health Organization (WHO): Novel coronavirus
- An open-access journal to accelerate peer review of COVID-19-related research:
  Rapid Reviews: COVID-19

Establishing the Evidence Base for Current and Future NASA Programs

Mary Wear, Ph.D.

NASA has exciting plans, from the Artemis Program with a return to the Moon by 2024, to Mars missions in the 2030's. NASA's prior human spaceflight experience provides valuable insight contributing to the success of future missions. Although the Apollo and Shuttle program mission profiles and vehicles are very different from the planned missions and vehicles, the biomedical data collected during those early missions provide the evidence base that NASA can use to inform the capabilities required for successful lunar and Mars missions.[1-4]

One area of focus is potential cardiovascular issues associated with transition to a partial gravity environment during planetary landings. Crewmembers will land, stay, and work on the Moon and Mars for extended periods in partial gravity (0.17 G on the Moon, 0.38 G on Mars). Prior knowledge from the Apollo landings is being used to inform a redefined risk, "Risk of Cardiovascular Adaptations Contributing to Adverse Mission Performance and Health Outcomes," for evaluation by NASA's Human System Risk Board (HSRB). This risk combines knowledge from several separate risks (cardiac rhythm problems, orthostatic intolerance during re-exposure to gravitational forces, and tissue degeneration due to radiation exposure) into one consolidated risk to address the multiple exposures and potential health outcomes. This use of prior mission data to create the evi-

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Establishing the Evidence Base for Current and Future NASA Programs continued

dence base for Artemis mission requirements is described in the article, "Apollo to Artemis: Mining 50-Year-Old Records to Inform Future Human Lunar Landing Systems" in the Lifetime Surveillance of Astronaut Health (LSAH) Newsletter, Volume 25, Issue 1, which was released in May 2020.[5]

A second area of focus is that one of the Commercial Crew Program (CCP) providers and the Orion Program designed their vehicles for water landings. Long duration spaceflight results in a confluence of risks, some of which impact performance of deconditioned crew on landing. The neurovestibular disturbances normally experienced during landing may be exacerbated during a water landing due to wave motion. To address the risks associated with water landings, information from multiple risks have been combined into the emerging "Risk to Vehicle Crew Egress Capability as Applied to Earth and Extraterrestrial Landings" for consideration by the HSRB. The existing risks being considered in this combined risk include:

- Injury from dynamic loads;
- Impaired control of spacecraft/associated systems and decreased mobility due to vestibular/sensorimotor alterations associated with spaceflight;
- Impaired performance due to reduced muscle size, strength, and endurance;
- Reduced physical performance capabilities due to reduced aerobic capacity;
- Orthostatic intolerance during re-exposure to gravity;
- Adverse outcomes due to inadequate human systems integration architecture.

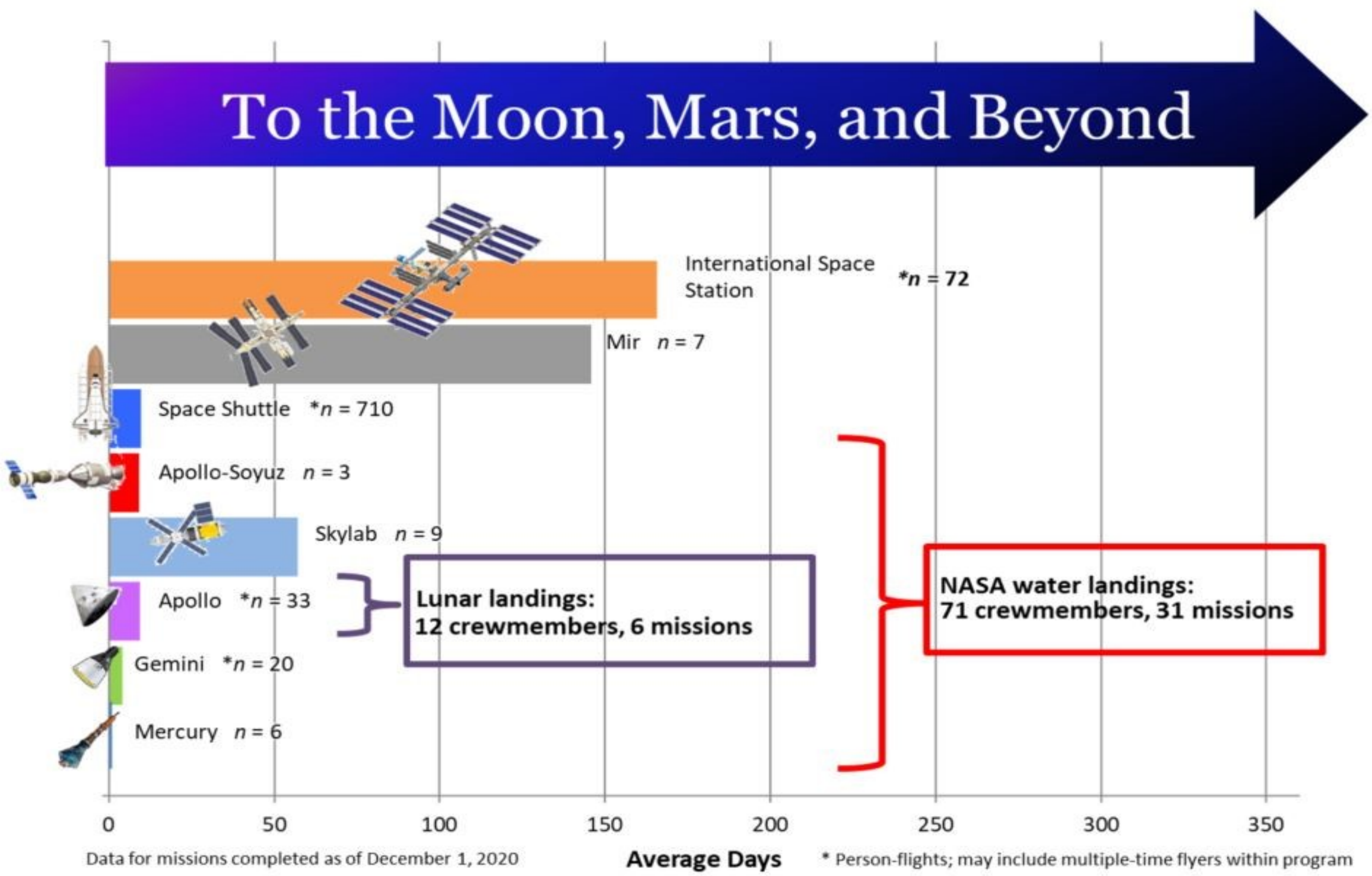

Figure 4.
Data for missions completed as of December 1, 2020

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Establishing the Evidence Base for Current and Future NASA Programs continued

The knowledge gained from all NASA's programs will be combined to assess the crew's ability to independently egress the vehicle and to perform post-landing (water or land) tasks in a timely manner. Both medical monitoring and research data are being used to evaluate the risks.

With each mission NASA undertakes, it adds to the biomedical evidence base. The entirety of knowledge gained from the beginning of the U.S. space program to present will be required to anticipate and address the needs of current and future programs. We are working to ensure the safety of the crewmembers and manage risks as we venture to the Moon, Mars, and beyond.

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Do you have a suggestion for an article or other information you would like us to include in the next Newsletter? Do you have any photos, news or updates you would like to share with the corps? We'd love to hear about it! Send suggestions, comments, or questions to
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FYI

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